WHAT IS CLAIMED IS:

1. A method for preparation of a composition comprising lipid-encapsulated therapeutic agent particles, said method comprising the steps of:

(a) combining a mixture of lipids comprising at least a first lipid component and a second lipid component with a buffered aqueous solution of a charged therapeutic agent to form an intermediate mixture containing lipid-encapsulated therapeutic agent particles, said first lipid component being selected from among lipids containing a protonatable or deprotonatable group that has a pKa such that the lipid is in a charged form at a first pH and a neutral form at a second pH, said buffered solution having a pH such that the first lipid component is in its charged form when in the buffered solution, said first lipid component being further selected such that the charged form is cationic when the charged therapeutic agent is anionic in the buffered solution, and anionic when the charged therapeutic agent is cationic in the buffered solution, and said second lipid component being selected from among lipids that prevent particle aggregation during lipid-therapeutic agent particle formation, and

(b) changing the pH of the intermediate mixture to neutralize at least some exterior surface charges on said lipid-encapsulated therapeutic agent particles to provide at least partially-surface neutralized lipid-encapsulated therapeutic agent particles.

2. The method of claim 1, wherein the therapeutic agent is a polyanionic nucleic acid.

3. The method of claim 2, wherein said composition consists essentially of lipid-nucleic acid particles, said particles having a size of from 70 nm to about 200 nm.

4. The method of claim 2, wherein said mixture of lipids in step (a) is a mixture of lipids in alcohol.

5. The method of claim 2, wherein the first lipid component is an amino lipid.

6. The method of claim 2, wherein the second lipid component is a polyethylene glycol-modified or polyamide oligomer-modified lipid.

7. The method of claim 6, wherein the second lipid component is a PEG-Ceramide.

8. The method of claim 6, wherein the first lipid component is an amino lipid.

9. The method of claim 2, wherein said lipids present in said lipid mixture comprises an amino lipid having a pKa of from about 5 to about 11, a neutral lipid, Chol and a PEG-modified or polyamide oligomer-modified lipid.

10. The method of claim 9, wherein said lipids are present in molar percents of about 25-45% neutral lipid, 35-55% Chol, 10-40% amino lipid and 0.5-15% PEG-modified or polyamide oligomer-modified lipid.

11. The method of claim 2, wherein said mixture of lipids comprises DODAP, DSPC, Chol and PEG-CerC14.

12. The method of claim 11, wherein said lipids are present in molar percents of about 25-45% DSPC, 35-55% Chol, 10-40% DODAP and 0.5-15% PEG-CerC14.

13. The method of claim 2, wherein said mixture of lipids comprises DODAP, POPC, Chol and PEG-CerC14.

14. The method of claim 2, wherein said mixture of lipids comprises DODAP, SM, Chol and PEG-CerC14.

15. The method of claim 2, wherein said nucleic acid is an antisense nucleic acid.

16. The method of claim 15, wherein said antisense nucleic acid contains linkages selected from the group consisting of phosphodiester, phosphorothioate, phosphorodithioate, boranophosphate, phosphoroselenate and amidate linkages.

17. The method of claim 2, wherein said nucleic acid contains exclusively phosphodiester linkages.

18. The method of claim 17, wherein said nucleic acid is an antisense nucleic acid.

19. The method of claim 17, wherein the buffered solution comprises 10 to 50 mM citrate or phosphate buffer.

20. The method of claim 2, wherein the nucleic acid contains at least some phosphorothioate or phosphorodithioate linkages.

21. The method of claim 20, wherein the buffered solution comprises 10 to 300 mM citrate or phosphate buffer.

22. The method of claim 2, wherein said nucleic acid is a ribozyme.

23. The method of claim 1, wherein said composition consists essentially of lipid-nucleic acid particles, said particles having a size of from 70 nm to about 200 nm.

24. The method of claim 1, wherein said mixture of lipids in step (a) is a mixture of lipids in alcohol.

25. The method of claim 1, wherein the first lipid component is an amino lipid.

26. The method of claim 1, wherein the second lipid component is a polyethylene glycol-modified or polyamide oligomer-modified lipid.

27. The method of claim 26, wherein the second lipid component is a PEG-Ceramide.

28. The method of claim 26, wherein the first lipid component is an amino lipid.

29. The method of claim 1, wherein said lipids present in said lipid mixture comprises an amino lipid having a pKa of from about 5 to about 11, a neutral lipid, Chol and a PEG-modified or Polyamide oligomer-modified lipid.

30. The method of claim 29, wherein said lipids are present in molar percents of about 25-45% neutral lipid, 35-55% Chol, 10-40% amino lipid and 0.5-15% PEG-Ceramide.

31. The method of claim 1, wherein said mixture of lipids comprises DODAP, DSPC, Chol and PEG-CerC14.

32. The method of claim 31, wherein said lipids are present in molar percents of about 25-45% DSPC, 35-55% Chol, 10-40% DODAP and 0.5-15% PEG-CerC14.

33. The method of claim 1, wherein said mixture of lipids comprises DODAP, POPC, Chol and PEG-CerC14.

34. The method of claim 1, wherein said mixture of lipids comprises DODAP, SM, Chol and PEG-CerC14.

35. The method of claim 1, wherein the pH is changed in step (b) to physiological pH.

36. The method of claim 1, wherein the step of changing the pH is performed using tangential flow dialysis.

37. A composition comprising lipid-therapeutic agent particles comprising a lipid portion and a charged therapeutic agent, said charged therapeutic agent being encapsulated in said lipid portion, wherein said lipid portion comprises at least a first lipid component and a second lipid component, said first lipid component being selected from among lipids containing a protonatable or deprotonatable group that has a pKa such that the lipid is in a charged form at a first pH and a neutral form at a second pH, and said first lipid component being further selected such that the charged form is cationic when the therapeutic agent is anionic and anionic when the therapeutic agent is cationic, and said second lipid component being selected from among lipids

that prevent particle aggregation during lipid-nucleic acid particle formation and which exchange out of the lipid particle at a rate greater than PEG-CerC20.

38. The composition according to claim 37, wherein at least some of the protonatable or deprotonatable groups disposed on the exterior surface of the particles have been neutralized.

39. The composition according to claim 38, wherein the therapeutic agent is anionic.

40. The composition according to claim 39, wherein the therapeutic agent is a polyanionic nucleic acid.

41. The composition according to claim 40, wherein the nucleic acid is an antisense nucleic acid.

42. The composition according to claim 40, wherein at least 50% of the nucleic acid in the composition is encapsulated within the particle.

43. The composition of claim 40, wherein at least 90% of the nucleic acid in the composition is encapsulated within the particle.

44. The composition of claim 40, wherein the nucleic acid has exclusively phosphodiester linkages.

45. The composition of according to claim 39, wherein the first lipid component is an amino lipid.

46. The composition of claim 45, wherein the second lipid component is a polyethylene glycol-modified or polyamide oligomer-modified lipid.

47. The composition of claim 39, wherein the second lipid component is a polyethylene glycol-modified or polyamide oligomer-modified lipid.

48. A composition comprising lipid-therapeutic agent particles comprising a lipid portion and a charged therapeutic agent, said charged therapeutic agent being encapsulated in said lipid portion, wherein said lipid portion comprises at least a first lipid component and a second lipid component, said first lipid component being selected from among lipids containing a protonatable or deprotonatable group that has a pKa such that the lipid is in a charged form at a first pH and a neutral form at a second pH, and said first lipid component being further selected such that the charged form is cationic when the therapeutic agent is anionic and anionic when the therapeutic agent is cationic, and said second lipid component being selected from among lipids that prevent particle aggregation during lipid-nucleic acid particle formation, said particles having a nucleic acid/lipid ratio of at least 10% by weight and a size of from about 70 to about 200 nm.

49. The composition according to claim 48, wherein at least some of the protonatable or deprotonatable groups disposed on the exterior surface of the particles have been neutralized.

50. The composition according to claim 49, wherein the therapeutic agent is anionic.

51. The composition according to claim 50, wherein the therapeutic agent is a polyanionic nucleic acid.

52. The composition according to claim 51, wherein the nucleic acid is an antisense nucleic acid.

53. The composition according to claim 50, wherein the nucleic acid has exclusively phosphodiester linkages.

54. The composition of according to claim 53, wherein the first lipid component is an amino lipid.

55. The composition of claim 54, wherein the second lipid component is a polyethylene glycol-modified lipid.

56. The composition of claim 53, wherein the second lipid component is a polyethylene glycol-modified lipid.

57. The composition of claim 53, wherein the lipid portion comprises a neutral lipid, an amino lipid, cholesterol and PEG-modified or polyamide oligomer-modified lipid, and wherein said lipids are present at molar percents of about 25-45% neutral lipid, 35-55% cholesterol, 10-40% amino lipid and 0.5-15% PEG-modified or Polyamide oligomer-modified lipid.

58. The composition of claim 53, wherein said lipid portion comprises DODAP, DSPC, Chol and PEG-CerC14.

59. The composition of claim 58, wherein the lipids are present in molar percents of about 25-45% DSPC, 35-55% Chol, 10-40% DODAP and 0.5-15% PEG-CerC14.

60. The composition of claim 53, wherein said lipid portion comprises DODAP, POPC, Chol and PEG-CerC14.

61. The composition of claim 53, wherein said lipid comprises of DODAP, SM, Chol and PEG-CerC14.

62. The composition according to claim 51, wherein at least 50% of the nucleic acid in the composition is encapsulated within the particle.

63. The composition of claim 51, wherein at least 90% of the nucleic acid in the composition is encapsulated within the particle.

64. The composition of claim 51, wherein said nucleic acid is a ribozyme.

65. The composition of according to claim 48, wherein the first lipid component is an amino lipid.

66. The composition of claim 65, wherein the second lipid component is a polyethylene glycol-modified or polyamide oligomer-modified lipid.

67. The composition of claim 48, wherein the second lipid component is a polyethylene glycol-modified or polyamide oligomer-modified lipid.

68. A composition in accordance with claim 48, wherein the lipid portion comprises a neutral lipid, an amino lipid, cholesterol and a PEG-modified or polyamide oligomer-modified lipid, and wherein said lipids are present at molar percents of about 25-45%

neutral lipid, 35-55% cholesterol, 10-40% amino lipid and 0.5-15% PEG-modified or polyamide oligomer-modified lipid.

69. A method for introducing a nucleic acid into a cell, comprising contacting a cell with a lipid-nucleic acid composition prepared according to claim 2 for a period of time sufficient to introduce the nucleic acid into said cell.

70. A method for the treatment or prevention of a disease characterized by aberrant expression of a gene in a mammalian subject comprising,

preparing a lipid-encapsulated therapeutic nucleic acid particle according to the method of claim 2, wherein the therapeutic nucleic acid component hybridizes specifically with the aberrantly expressed gene; and

administering a therapeutically effective or prophylactic amount of the particle to the mammalian subject, whereby expression of the aberrantly expressed gene is reduced. .

71. The method of claim 70, wherein the gene is selected from among ICAM-1, c-myc, c-myb, ras, raf, erb-B-2, PKC-alpha, IGF-1R, EGFR, VEGF and VEGF-R-1.

72. The method of claim 70, wherein the disease is a tumor.

73. The method of claim 70, wherein the disease is characterized by inflammation.

74. The method of claim 70, wherein the disease is an infectious disease.

75. The method of claim 70, wherein the therapeutically effective amount of the particle is administered to the mammalian subject by intravenous injection.

76. The method of claim 75, wherein the therapeutically effective amount of the particle is administered to the mammalian subject by intravenous injection at an injection site, and wherein the disease is localized at a disease site distal to the injection site.

77. The method of claim 70, wherein the nucleic acid comprises exclusively phosphodiester linkages.

78. A method of preventing expression of a disease-associated gene in a mammalian cell comprising,

preparing a lipid-therapeutic oligonucleotide particle according to claim 2 containing an antisense therapeutic agent; and

exposing the mammalian cell to the lipid-therapeutic oligonucleotide particle for a period of time sufficient for the therapeutic oligonucleotide component to enter the cell;

wherein the antisense therapeutic agent has a sequence complementary to the disease-associated gene and reduces the production of the gene product of the disease-associated gene in the cell.

79. A pharmaceutical composition comprising lipid-therapeutic agent particles prepared according to claim 1 and a pharmaceutically acceptable carrier.

80. The pharmaceutical composition according to claim 79, wherein the therapeutic agent is a polyanionic nucleic acid.

81. The pharmaceutical composition according to claim 80, wherein the nucleic acid is an antisense nucleic acid.

82. A method for treatment or prevention of a disease characterized by aberrant expression of a gene in a mammalian subject comprising, administering to mammalian subject a composition comprising lipid-encapsulated nucleic acid particles, wherein the lipid-encapsulated nucleic acid particles contain at least 10% by weight of nucleic acids and the nucleic acids have exclusively phosphodiester linkages.

83. A composition comprising lipid-encapsulated nucleic acid particles, wherein the lipid- encapsulated nucleic acid particles contain at least 10% by weight of nucleic acids and the nucleic acids have exclusively phosphodiester linkages.